REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 41.50(b)(1), are respectfully requested.

On August 28, 2008, a Decision on Appeal was mailed to the Applicants. In this decision, the Board of Patent Appeals and Interferences affirmed the Examiner's rejections of claims 3-5, 17, 22-24 and 28-40 and reversed the rejection of claims 14, 18, 19 and 25-27. The Board also entered a new ground of rejection of claims 14, 18, 19 and 25-27.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 14, 18, 19 and 25-27 stand rejected under 35 U.S.C. § 103(a) as purportedly obvious in view of Ebert (U.S. Pat. No 5,662,925), Cormier (U.S. Pat. No. 6,203,817) and Ke (U.S. Pat. No. 6,323,232). This rejection is respectfully traversed.

The Board stated that:

> It would have been obvious to a person of ordinary skill in the art to combine Ebert's device with the transdermal administration of lasofoxifene suggested by Cormier and Ke because Ebert stated that the disclosed device is useful for administering a variety of agents, including estradiol (Ebert, col. 4, l. 20).

The Board bases its argument in combining these publications on the assertion that Cormier and Ke suggest the transdermal administration of lasofoxifene. And based on this assertion, the Board concludes that one of ordinary skill in the art would then combine Cormier and Ke with the transdermal device in Ebert to render the invention set forth in claims 14, 18, 19 and 25-27 obvious.

This assertion, however, fails to take into account the chemical properties of compounds and how these properties dictate their formulation. Moreover, this argument is based on the false presumption that drugs of the same pharmacological class possess similar chemical properties that would allow their interchangability in transdermal formulations.

It is a well-established principle of patent law that compounds of similar *structure* are presumed to have similar properties. *See, In re Dillon*, 919 F.2d 688, 692-693; 16 U.S.P.Q. 2d 1897, 1901 (Fed. Cir. 1990). However, there is *no* legal basis for presuming the converse, *i.e.*, that compounds with similar pharmacological activities necessarily have similar chemical structures or characteristics. Indeed, the opposite is true. *See, e.g., In re Jezl*, 396 F.2d 1009, 1012; 158 U.S.P.Q. 98, 99-100 (CCPA 1968) ("the mere inclusion of several compounds in a list of compounds...does not necessarily establish that each of those compounds is equivalent to the others for all purposes."). It is well known in the art that a compound's pharmacological classification is based on the behavior a compound exhibits in the human body and not on its chemical make-up. For example, antiestrogenic compounds such as lasofoxifene have a single characteristic in common: the fact that they work against the effect of estrogen *in vivo*. As a result of this activity, they are listed together under the pharmacologic class of antiestrogenic compounds.

The Board's rejection, however, assumes that because Cormier and Ke list antiestrogenic compounds in their specifications, then any reference mentioning a compound having estrogenic properties could be combined with these publications on that basis to render an invention obvious. This assumption though fails to take into account several points that one of ordinary

skill in the art would consider vital in formulating a drug delivery device and method of use relating to such a device.

In order to demonstrate these points and that it would not be possible to predictably combine Cormier, Ke and Ebert with a reasonable expectation of success to yield the invention set forth in claims 14, 18, 19 and 25-27, the declaration of Dr. Andrew Coop is submitted under 37 C.F.R. 1.132 with this Reply. As Dr. Coop notes, the chemical make up of the compounds described in Cormier (that include tamoxifen and raloxifene) is significantly different from that of lasofoxifene, Likewise, Dr. Coop notes that the chemical make up of the antiestrogenic compounds listed in Ke (droloxifene and idoxifene) is significantly different from that of lasofoxifene. These differences include differing chemical structures and functional groups composing the compounds. Those differences in turn affect properties such as the stability of the active ingredient, the stability of the adjuvant in combination with the active ingredient, the phase distribution of the compound within a matrix, the release of the compound from the matrix, pH and bioavailability.

Consequently, even though both Cormier and Ke list tamoxifen and raloxifene, neither Cormier nor Ke suggest to one of ordinary skill in the art that any other antiestrogenic compound may be interchangeable for purposes of formulating the transdermal device described in Cormier or even the device in Ebert merely because Ebert lists estradiol in the specification.

As Dr. Coop notes, each of the differences in chemical make up of these compounds introduces unpredictability to the use of these compounds, especially with regard to formulations. The transdermal device in Cormier is an inherently unpredictable system based on the differences in how a drug would interact with the other components in the formulation that

come into contact within the device itself. This unpredictability is magnified by the unpredictability of the kinetics by which a drug passes out of the device and into the patient. In fact, the unpredictability of the transdermal device in Cormier is the likely reason that the inventors limited the antiestrogenic compounds in the specification to the relatively well-characterized compounds tamoxifen and raloxifene.

The issue of unpredictability is magnified with regard to the assertion that the Ke publication suggests transdermal administration of lasofoxifene that would render obvious the device set forth in the currently pending claims. For example, Ke states that "[f]or purposes of transdermal (e.g. topical) administration, dilute sterile, aqueous or partially aqueous solutions (usually in about 0.1% to 5% concentration), otherwise similar to the above parenteral solutions, are prepared" (*see* col. 37, lines 49-52). This statement merely describes topically administering lasofoxifene in aqueous form. It does not describe or suggest the transdermal delivery of lasofoxifene using a transdermal device as set forth in the instant claims. In fact, as established by Dr. Coop, one of ordinary skill in the art would not recognize that the topical administration of an aqueous solution of lasofoxifene would in any way predictably dictate that the same concept would translate to the transdermal delivery of lasofoxifene using the device and methods of the instant claims. As Dr. Coop notes, the topical administration of an aqueous solution of any drug would not be suggestive of whether that drug could be incorporated into a transdermal delivery device because many unpredictable factors must be taken into account not only with the drug, but also with the device itself.

Similarly, one of ordinary skill could not reasonably conclude from the mere suggestion of a formulation containing antiestrogenic compounds, that the trandermal device described in

Ebert could be used with lasofoxifene merely because Ebert lists the hormone, estradiol, in the specification. And as Dr. Coop notes, the very fact that several assumptions must be made based on the unpredictable components would not lead one of ordinary skill in the art to conclude that the lasofoxifene could be successfully and predictably used in a transdermal drug delivery device based on their established functions.

Accordingly, it is submitted that the presently claimed invention is not obvious over the cited publications in view of the multitude of variables required to be considered in formulating a transdermal device for the delivery of lasofoxifene. Because of that unpredictability, the presently claimed invention does not arise from the predictable use of prior art elements based on their established functions. The extent of this unpredictability would, in turn, dissuade one of skill in the art from combining the references to claim the invention as the Applicants have. For all these reasons, it is respectfully requested that this rejection be withdrawn.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order and such action is respectfully requested.

In the event that there are any questions relating to this Amendment or to the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (202) 373-6000 so that prosecution of the application may be expedited.

The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-4047.

Respectfully submitted,

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Date: October 27, 2008

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